

REMARKS

Claims 19 and 21-23 are amended. Claim 24 is cancelled without prejudice or disclaimer. Claims 1-23 and 25-36 are currently pending in this application. Claims 1-18 and 25-36 are withdrawn from consideration.

Claims 19 and 21-23 are amended to delete the phrase "or a derivative thereof" in relation to the nucleic acid molecule. No new matter is added by the amendment.

Withdrawal of the rejection of claims 19-24 under 35 U.S.C. §103 from the previous Office Action is acknowledged.

CLAIM REJECTIONS - 35 USC § 112

Claims 19-24 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The Office Action alleges that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. The Examiner states that the specification, while being enabling for SEQ ID NO: 1 and SEQ ID NO: 2, does not reasonably provide enablement for any nucleic acid sequence exhibiting ROS repressor and ROS operator binding activity as broadly claimed.

Applicants respectfully traverse the rejection.

Claims 19, 21 and 22-24 are amended to delete the phrase "or a derivative thereof" in relation to the nucleic acid molecule, therefore the Examiner's statement that millions of synthetic derivations of ROS repressors will need to be evaluated by the skilled person for their function as ROS repressors is no longer applicable.

Claim 19, as amended above, is directed to a method for selectively controlling the transcription of a gene of interest by crossing a first plant with a second plant. The first plant comprises a first genetic construct comprising a regulatory region operatively linked to a gene of interest and a ROS operator sequence. The second plant comprises a second genetic construct comprising a regulatory region in operative association with a nucleic acid molecule encoding a ROS repressor. The ROS repressor exhibits both ROS operator binding activity and ROS repressor activity. The progeny obtained by the cross comprises both the first and second genetic construct and expression of the second genetic construct represses expression of the first genetic construct. Claim 20 is dependent on claim 19.

Claims 21, 22 and 23 are similar to claim 19, however the first and second genetic constructs are introduced into a single plant instead of crossing two plants.

Claim 24 is cancelled above without prejudice or disclaimer, therefore the rejection of this claim is moot.

The present invention provides a method for the regulation of gene expression within plants using ROS repressors. The method utilizes two genetic constructs; the first construct comprising a regulatory region operatively linked to a gene of interest and a ROS operator sequence, and the second construct comprising a second regulatory region in operative association with a nucleic acid molecule encoding a ROS repressor. The ROS repressor exhibits both ROS operator binding activity and ROS repressor activity, such that expression of the second genetic construct produces a ROS repressor protein which binds to the ROS operator sequence and represses expression of the gene of interest, thereby controlling expression of the gene of interest.

Enablement

As part of the *quid pro quo* of the patent bargain, the applicant's specification must enable one of ordinary skill in the art to practice the full scope of the claimed invention.... That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending up on the

predictability of the art. *AK Steel corp. v. Sollac*, 344 R.3d 1234, 1244, 68 USPQ2d 1280 (Fed. Cir 2003).

Applicants submit that the present disclosure provides adequate guidance in the way of examples, which enable one of ordinary skill in the art to practice the full scope of the claimed method of the present invention. Example 1 of the specification describes optimization of a *ros* nucleotide sequence derived from *Agrobacterium tumefaciens* by examining the coding region of the nucleic acid sequence of the ROS repressor and modifying the sequence to optimize for expression of the gene in plants, using a known procedure as outlined by Sardana et al. (Plant Cell Reports 15:677-681; 1996). A table of codon usage from highly expressed genes of dicotyledonous plants was compiled using the known data of Murray et al. (Nuc. Acids Res. 17:477-498; 1989). It would have been well within the artisan's knowledge of the prior art and routine experimentation to optimize other *ros* nucleotide sequences for use in the method of the present invention.

In Example 2, ROS repressor constructs that express either "wild type ROS" (SEQ ID NO: 1; Figure 1A) or "synthetic ROS" (SEQ ID NO: 2; Figure 1B) were prepared and used to transform plants to obtain the ROS parent. Transgenic lines containing GUS reporter constructs (GUS parent) crossed with transgenic lines containing ROS repressor constructs (ROS parent) exhibit reduced expression of GUS. Results of the cross are presented in FIG. 9 and demonstrate ROS repression of a gene of interest. The results in FIG. 9A demonstrate that GUS activity is detected in the GUS parent but not in the ROS parent (which does not comprise the GUS construct), or in the progeny of the cross between the ROS and GUS parent. The parent plants each expressed either GUS or ROS RNA as expected (FIG. 9B), yet no GUS RNA was detected in the progeny arising from a cross between the ROS and GUS parents. Southern analysis of the progeny of the cross between the GUS and ROS parents indicates that the progeny plant from the cross between the ROS and GUS parent comprised genes encoding both GUS and ROS (FIG. 9C).

The Office Action states that in the previous office action, page 5, peer-reviewed literature was cited that demonstrated the unpredictability in the functioning of ROS repressors and that the claim breadth would require the evaluation of ROS repressors from thousands of species, as well as millions of synthetic derivations for their function as ROS repressors.

The peer reviewed article referred to by the Examiner (Archdeacon et al. (2000 FEMS Microbiology Letters 187:175-178, 2000) relates to a mutant ROS repressor from *Agrobacterium tumefaciens* with a Arg to Cys conversion at amino acid residue 125. ROS bearing this mutation was unable to bind to the ROS-box and therefore falls outside the scope of the present claims which specifies that the ROS repressor exhibits both ROS operator binding activity and ROS repressor activity. Applicant's respectfully submit that a person skilled in the art would be readily able to select nucleic acid molecules encoding ROS repressor proteins known to have ROS operator binding activity as well as ROS repressor activity for use in the method of the present claims. ROS repressors that satisfy the criteria defined in the claims are well known in the art, and reference is made to a selection of such repressors in the application (page 14, lines 3-13, and Figure 1). As claims 19-23 specify that the nucleic acid molecule encodes a ROS repressor exhibiting both ROS operator binding activity and ROS repressor activity, a skilled person would not have been lead to use the mutant ROS repressor disclosed in Archdeacon et al.

Additionally, according to *Capon v. Eshar*, (citing *In re Angstadt*, 537 F.2d 498, 504 CCPA 1976) "It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention."

In view of the above comments, withdrawal of the rejection of claims 19-24 under 35 U.S.C. 112, first paragraph for failing to comply with the enablement requirement is respectfully requested.

Written Description

Claims 19-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Office Action states that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully traverse the rejection.

The subject matter defined in claims 19-24 is described above.

Applicant submits that the present disclosure is of such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention. Example 1 of the specification describes optimization of a *ros* nucleotide sequence derived from *Agrobacterium tumefaciens*. In Example 2, ROS repressor constructs that express either "wild type ROS" (SEQ ID NO: 1; Figure 1A) or "synthetic ROS" (SEQ ID NO: 2; Figure 1B) were prepared and used to transform plants to obtain the ROS parent. Transgenic lines containing GUS reporter constructs (GUS parent) crossed with transgenic lines containing ROS repressor constructs (ROS parent) exhibit reduced expression of GUS. Results of the cross are presented in FIG. 9 and demonstrate ROS repression of a gene of interest. The results in FIG. 9A demonstrate that GUS activity is detected in the GUS parent but not in the ROS parent (which does not comprise the GUS construct), or in the progeny of the cross between the ROS and GUS parent. The parent plants each expressed either GUS or ROS RNA as expected (FIG. 9B), yet no GUS RNA was detected in the progeny arising from a cross between the ROS and GUS parents. Southern analysis of the progeny of the cross between the GUS and ROS parents indicates that the progeny plant from the cross between the ROS and GUS parent comprised genes encoding both GUS and ROS (FIG. 9C). The Examples given in the description therefore clearly indicate to persons skilled in the art that as of the filing date the applicant had invented what is now claimed in accordance with *Eiselstein v. Frank*, 52 F.3d 1035, 1038, 34 USPQ2d 1467, 1470 (Fed. Cir. 1995).

Furthermore, Applicant submits that the case law supports the position that claims should not be invalidated based on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. As noted in *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc* (424 F.3d 1336, 1345; Fed. Cir. 2005), it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation. Applicant submits that this threshold has been met with the present description.

Applicant's arguments submitted in response to the non-final office action dated July 13, 2006, were deemed not persuasive, alleging, in view of *University of California v. Lilly*, that the disclosure of four SEQ ID NOS does not adequately represent literally, or otherwise the ROS repressors from thousands of species, as well as millions of synthetic derivations that function as ROS repressor as claimed by Applicant.

In *Falko-Gunter Falkner, et al. v. Stephen C. Inglis et al.* 05-1324 (Interference No. 105,187) (Fed Cir 2006), the court found that reliance on *University of California v. Lilly* in that particular case was inappropriate. In *Lilly*, the cDNA for human insulin had never been characterized. As noted in *Falko-Gunter Falkner, et al. v. Stephen C. Inglis et al.* 05-1324 (Interference No. 105,187; Fed Cir 2006) "The 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge." In that case, the court found that the Board's rule that the nucleotide sequences of the chimeric genes at issue must be fully presented, although the nucleotide sequences of the component DNA was known, was an inappropriate generalization.

Similarly, satisfaction of the written description in the present case does not require that the nucleotide sequence for every ROS repressor be included in the specification.

Applicants respectfully submit that the present claims are not directed to a new product (ROS repressor), but are rather directed to a method of using *known* ROS repressor sequences in a new way to control gene expression in plants. A person skilled in the art to which the specification pertains, or with which it is most nearly connected, would be readily

able to identify *known* nucleic acid molecules that encode a ROS repressor exhibiting both ROS operator binding activity and ROS repressor activity, especially as the present specification discloses a number of possible ROS repressors (see para. 65) including:

...microbial ROS repressors, for example but not limited to ROSAR (*Agrobacterium radiobacter*, Brightwell et al. (1995) *Mol. Plant Microbe Interact.* 8: 747-754), MucR (*Rhizobium meliloti*; Keller M et al., (1995) *Mol. Plant Microbe Interact.* 8: 267-277), and ROSR (*Rhizobium elti*; Bittinger et al., (1997) *Mol. Plant Microbe Interact.* 10: 180-186; also see Cooley et al. 1991, *J. Bacteriol.* 173: 2608-2616; Chou et al., 1998, *Proc. Natl. Acad. Sci.*, 95: 5293; Archdeacon J et al. 2000, *FEMS Microbiol Let.* 187: 175-178; D'Souza-Ault M. R., 1993, *J Bacteriol* 175: 3486-3490.

Applicants submit that the skilled artisan may also routinely carry out a BLAST type search to determine other ROS repressor nucleic acid sequences that may be utilized in the method of the present invention. A person of ordinary skill in the art would clearly have possessed such knowledge, and would be readily able to make and use the method of the present invention, without undue experimentation; Applicant should be entitled to fair protection for their invention.

In the present invention, a variety of ROS repressors are known in the art. Furthermore, the function of these repressors is established and well known in the art. The use of a plant optimized ROS repressor to control expression of a desired sequence, as defined in the claims, has not been disclosed or exemplified, and this is now provided with the present invention. To limit the method to exemplified ROS sequences would permit a potential infringer to follow the methods described in the specification and use an equivalent ROS sequence to arrive at the same invention. Applicants respectfully submits that the function of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the subject matter claimed by him; the description of the present application readily fulfills this requirement.

In view of the above comments, Examiner is respectfully requested to withdraw the rejection of claims 19-24 under 35 U.S.C. 112, first paragraph for failing to comply with the written description requirement.

Reconsideration and allowance of this application are respectfully requested in view of the amendments and remarks above. It is believed that the application is now in condition for allowance, and such action is respectfully requested. If a telephone conference would be of assistance in advancing the prosecution of the subject application, the Examiner is invited to contact applicant's undersigned attorney at the number provided below.

Respectfully submitted,

A handwritten signature in cursive script, reading "Kathy Smith Dias", is written over a horizontal line.

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